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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,831	08/18/2000	C. Alexander Turner JR.	LEX-0035-USA	6428

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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/641,831	TURNER ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2003 has been entered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

3. Claims 1-12 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific or well-established utility.

The claims are drawn to isolated nucleic acids comprising the sequence of SEQ ID NO: 1, 3, or 5 and nucleic acids encoding the amino acid sequence of SEQ ID NO: 2, 4 or 6. The specification refers to these nucleic acids as encoding NHPs (novel human proteins). The claimed polynucleotides are not supported by either a specific and substantial asserted utility or a well-established utility. The specification fails to provide objective evidence of any activity for the encoded polypeptides. Rather, the specification indicates that homology studies show that the putative proteins have identity with "a variety of putative secreted proteins, a tyrosine phosphatase, several human LIM proteins, as well as several cancer (colon, renal, and lung) associated antigens" (page 12). It is further stated that the NHPs "share structural motifs typical of

the human APXL protein- a protein that is similar to a Xenopus amiloride sensitive sodium channel" (page 2). While the specification states that the sequences of the polynucleotides have homology to other known proteins, the specification does not set forth a specific level of sequence identity shared, over the complete sequence, between the claimed polynucleotides and known polynucleotides encoding transporter proteins. Identity of a polynucleotide sequence to other known polynucleotides does not by itself establish that a polynucleotide will encode for a product having the same activity as the known polynucleotides because a change at even a single amino acid position may affect a proteins function and a change at a single nucleotide position may affect the ability of a polynucleotide to encode for a polypeptide. Furthermore, no information is provided regarding the conservation of any particular domains which are required for transporter function or which are characteristic of specific types of transporter proteins. Accordingly, there is no evidence of record to suggest that the claimed polynucleotides do in fact encode for polypeptides a particular activity. In addition, the specification does not distinguish between which polynucleotides have identity to APXL, which have identity to "secreted proteins", which have identity to a tyrosine phosphatase, which have identity to a LIM protein, and which have identity to a cancer antigen. Moreover, these types of proteins fall into very general classes of proteins and are not considered to constitute a specific activity for utility purposes. The specification (for example, 12) suggests that the claimed polynucleotides could be used for therapeutic purposes or for diagnosis of disease. However, no specific diseases have been identified which are correlated with expression of the claimed polynucleotides. Clearly, further research

would be required to identify a disease for which the encoded protein is involved and for which treatment with the encoded proteins would be effective or for which detection of expression of SEQ ID NO: 1, 3 or 5 would be informative. As stated in Brunner v. Manson, 383 U.S. 519 535-536, 148 USPO 689, 696 (1966) " a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". The specification (see, for example, pages 30, 35 and 38) further asserts that the polynucleotides of SEQ ID NO: 1, 3 and 5 and the proteins of SEQ ID NO: 2, 4 and 6 can be used in drug screening methods. However, because the specification has not established that the proteins of SEQ ID NO: 2, 4 and 6 have a functional activity, the general concept of using any compound for the purposes of screening for agents which bind this compound is not considered to be a specific utility. While nucleic acids comprising SEQ ID NO: 1, 3 and 5 could be expressed to obtain protein for use in research aimed at determining or characterizing the polypeptides function, such use is general, rather than specific and substantial. Support for an asserted utility that is specific and substantial would require, for example, a showing of a particular function for an encoded polypeptide. Merely identifying and studying the properties of a polypeptide or the diseases in which a polypeptide may be involved does not constitute a "real world" context of use. Accordingly, the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, or credible asserted utility or well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

RESPONSE TO ARGUMENTS

4. In the response filed February 13, 2003, Applicants assert that the rejection implies that the use of the abbreviation NHP for novel human proteins is indicative of a lack of understanding or knowledge on the part of Applicant. Applicant also asserts that the Office action implies that because Applicant's sequence is novel, it lacks utility. Applicants interpretation of the previous Office actions is in error. Applicant's have mischaracterized the rejection in that there is simply no discussion whatsoever in any of the Office actions which would imply that the invention lacks novelty because Applicants use the terminology NHP or because the sequences are "novel."

Applicants provide statements regarding the various tissues in which the claimed NHP is expressed. It is unclear as to how Applicant's are relying on this expression data to establish a utility for the claimed invention. With respect to the expression of NHP proteins in particular tissues, the previous Office action addressed Applicant's arguments that "(k)nowing that a given gene is not expressed in a medically relevant tissue provides an informative finding of great value to the industry by allowing for the

more efficient deployment of expensive drug discovery resources." As discussed previously, these arguments are not persuasive because the disclosed nucleic acids have not been shown to be associated with any particular disease. While the finding that a gene is not expressed in a specific tissue is a valid research result, this information is useful only as a research tool to lead one to perform additional research. There is no evidence in the specification that any of the claimed nucleic acids are not expressed in any single specific tissue and/or are associated with the occurrence of a specific disease. It has not been established that the claimed nucleic acids could be used for the diagnosis of a specific disease or for the development of drugs to treat a particular disease. Clearly further research would be required to identify a disease, if one exists, in which expression or lack of expression of the disclosed nucleic acids are associated.

Applicants state that "the Action seems to be requiring Applicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides." However, Applicants have again mischaracterized the Office action. There are clearly no statements in any of the previous Office actions requiring Applicants to show evidence that the protein encoded by the claimed nucleic acids have a specific biological activity. The Office action discusses the fact that one means of establishing the utility of a nucleic acid is by setting forth a specific biological activity for the protein that is encoded by the nucleic acid. The specification as originally filed asserts that the nucleic acids discussed therein have functional activities such as

having APXL activity, proteins which have identity to "secreted proteins", proteins which have identity to a tyrosine phosphatase, proteins which have identity to a LIM protein, and proteins which have identity to a cancer antigen. However, the originally filed specification does not clarify which nucleic acids encode for which biological activities. Since the specification does not clearly set forth the function of the protein encoded by each nucleic acid, the specification has not described a specific utility for each nucleic acid and has not adequately taught one of skill in the art how to use the claimed nucleic acids. Further, the functional activity of the encoded protein was discussed in the previous Office action because Applicant's response raised the issue of the biological activity of the protein encoded by the claimed nucleic acids. In particular, in the response of Paper No. 9, Applicants state that one of the nucleic acids encodes for a protein having an amino-terminus characteristic of APXL and shroom related proteins. However, as previously discussed, there is no evidence of record to indicate that the presence of this amino-terminus alone would indicate to one of skill in the art that the presently claimed nucleic acid encodes for a APXL protein and that the encoded protein would have a specific activity and well known use. Applicants response of Paper No. 9 also asserted that one of the claimed nucleic acids encodes for a protein having an amino acid terminus shared with "shroom related proteins". However, the specification as originally filed does not teach that the claimed nucleic acids encode for "shroom related proteins". The specification as originally filed must teach the use of the claimed nucleic acids. Applicants statement that the claimed nucleic acid may encode for a protein whose role is "most likely" to anchor the complex to the membrane clearly

emphasizes the uncertainty in determining the function and activity of the encoded protein. Further, the specification as originally filed does not appear to state that the claimed nucleic acids are useful for encoding proteins that have the functional activity of anchoring a macromolecular complex to a membrane. Again, the utility of the claimed nucleic acid must be set forth in the originally filed specification. As is clear from the above discussion, the Office did not require that Applicants establish a biological activity for the encoded protein. The Office action simply addressed Applicant's assertions set forth in the specification and in the response of Paper No. 9 that Applicant's themselves were relying on an asserted biological activity of the encoded protein as a means to establish utility.

In the response of February 13, 2003, Applicants further traverse the rejection by arguing that gene chips are available in the public domain and that several companies have utilized gene sequences and fragments in gene-chip and non-gene chip formats. Applicants assert that this establishes a real world utility for gene sequences and fragments. These arguments have been fully considered but are not persuasive because while a gene chip itself has utility, uncharacterized gene sequences and fragments thereof do not have a well known established or specific and substantial utility. Gene sequences and fragments thereof may be used in gene-chip and non-gene chip formats to further study the function of nucleic acids. However, studying the expression pattern of uncharacterized nucleic acids and identifying nucleic acids which hybridize to uncharacterized genes constitutes further research to try to determine the

biological properties or functional activities of a nucleic acid. The use of a nucleic acid for further research is not considered to be a "real world" utility.

Applicants state that the claimed nucleic acids serve as markers useful for determining the genomic structure of a human chromosome. However, the ability of a nucleic acid to hybridize to a specific chromosome is a property characteristic of a large class of nucleic acids. Such a utility is considered to be general and is not a specific and substantial utility. Applicants state that the property of a nucleic acid to localize a specific region of the human chromosome is a utility not shared by virtually any other nucleic acid sequences and thereby such a marker can be used to map a specific locus of the human genome. It is stated that the claimed nucleic acids hybridize to given regions on chromosome 4, such that different portions of SEQ ID NO: 1 hybridize to distinct sequences within a 103,765 bp clone. Applicants thereby conclude that the sequences of the present invention have utility for mapping a gene product to the chromosome and in the identification and biological validation of exon/intron splice junctions. These arguments have been fully considered but are not persuasive for the following reasons. Firstly, it is noted that the originally filed specification states generically that the nucleic acids may be used for mapping and for determining intron/exon boundaries. Yet, there are no teachings provided in the specification as originally filed as to which chromosome and which specific gene the nucleic acids of SEQ ID NO: 1, 3 or 5 hybridize. Accordingly, the use of the claimed nucleic acids to detect chromosome 4 and to identify particular exons or introns within a clone obtained from chromosome 4 is not a utility set forth in the specification as originally filed.

Applicants may not rely on post-filing date research to establish a utility. The utility must be clearly and specifically set forth in the application as originally filed. Secondly, Applicants have not identified a specific gene to which SEQ ID NO: 1, 2 o4 3 hybridizes. It is a general property of nucleic acids that they may be used to hybridize to themselves and to hybridize to the chromosome from which they are derived. Accordingly, the use of the presently claimed nucleic acids for this purpose does not provide a specific and substantial utility. For these reasons, it is maintained that the claimed nucleic acids do not have a readily applicable, real-world utility.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

August 20, 2003

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER